FIG. 1-1

Human Basic Fibroblast Growth Factor

```
        10         20         30         40         50         60         70
AATTCATGCC TCTTTCTCTC CTTTTGTTGG TAGACGACTT CAGCCTCTGT CCTTTAATTT TAAAGTTTAT

        80         90        100        110        120        130        140
GCCCCACTTG TACCCCTCGT CTTTTGGTGA TTTAGAGATT TTCAAAGCCT GCTCTGACAC AGACTCTTCC

       150        160        170        180        190        200        210
TTGGATTGCA ACTTCTCTAC TTTGGGGTGG AAACGGCTTC TCCGTTTTGA AACGCTAGCG GGGAAAAAAT

       220        230        240        250        260        270        280
GGGGGAGAAA GTTGAGTTTA AACTTTTAAA AGTTGAGTCA CGGCTGGTTG CGCACGAAAA GCCCCCCAGT

       290        300        310        320        330        340        350
GTGGAGAAAG CCTAAACTTT GTTTGGGTTG TGGGGGGGTT GGGTGGGGGT GACTTTTGGG GGATAAGGGG

       360        370        380        390        400        410        420
CGGTGGAGCC CAGCGAATGC CAAAGCCCTG CCGCCGCCTC CGACGCGCGC CGCCCGCCCC TCGCCTCTCC

       430        440        450        460        470        480        490
CCCGCCCCCG ACTGAGCCCG CGCTCCCCGC CGGACTGATG TCGCCGCGTT CTGTGTTGTG CCCGAAGCCG

       500        510        520        530        540        550        560
CCGAACTCAG AGCCCGGCCC CAGAAAACCC GAGCGAGTAG GGCGCGGCGC GCAGGAGCGA CGAGAACTGG

       570        580        590        600        610        620        630
GGGCGCGGGA GGCTGGTGGG TGTGGGGGGT GGAGATGTAG AAGATGTGAC GCCGCGGCCC CGCCGGTGCC

       640        650        660        670        680        690        700
AGATTAGCGG ACCGCTCCCC GCGGTTGCAA CGGGATCCCG GGCGCTGCAG CTTGGGAGGC CGCTCTCCCC

       710        720        730        740        750        760        770
AGGCGGCGTC CGCCGGAGACA CCGATCTGTG AACCCCAGGT CCCCGGCCGC CGGCTCGCCG CGCACCAGGG

       780        790        800        810        820        830        840
GCCGGCGGAC AGAAGAGCGG CCGAGCGGCT CGAGGCTGGG GGACCGCGGG CGCGCCCCCG CGCTGCCGGG

       850        860        870        880        890        900        910
CGGGAGCGTG CGGCGCTGGG GAGCGGGCCG TGCCCGGAGC GGGTTCGAGG CGCGCGCCTG CGCCGCCGGA

       920        930        940        950        960
CGGCGGCTCC GCGCCCCGCT CCAGTGGCTC GGCGATCTGG GCTGGCGCCG GCAGCGAGC ATG GCA GCC
                                                      Met Ala Ala

    984                989                1014               1039
GGG AGC ATC ACC ACG CTG CCC GCC TTG CCC GAG GAT GGC GGC AGC GCC TTC CCC
Gly Ser Ile Thr Thr Leu Pro Ala Leu Pro Glu Asp Gly Gly Ser Gly Ala Phe Pro

       1044               1059               1074               1089
CCC GGC CAC TTC AAG GAC CCC AAG CGG CTG TAC TGC AAA AAC GGG GGC TTC TTC CTG
Pro Gly His Phe Lys Asp Pro Lys Arg Leu Tyr Cys Lys Asn Gly Gly Phe Phe Leu
```

FIG. 1-2

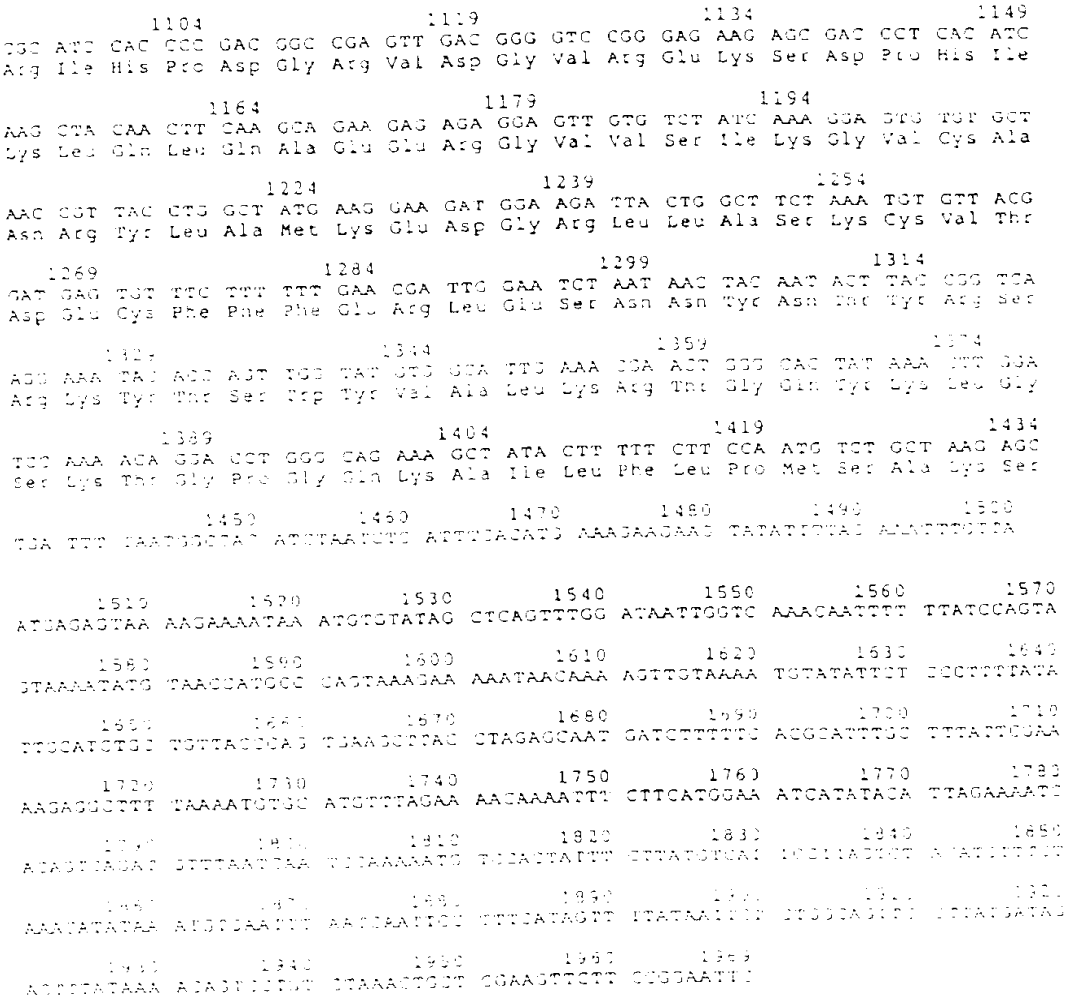

1104 1119 1134 1149
CGC ATC CAC CCC GAC GGC CGA GTT GAC GGG GTC CGG GAG AAG AGC GAC CCT CAC ATC
Arg Ile His Pro Asp Gly Arg Val Asp Gly Val Arg Glu Lys Ser Asp Pro His Ile
1164 1179 1194
AAG CTA CAA CTT CAA GCA GAA GAG AGA GGA GTT GTG TCT ATC AAA GGA GTG TGT GCT
Lys Leu Gln Leu Gln Ala Glu Glu Arg Gly Val Val Ser Ile Lys Gly Val Cys Ala
1224 1239 1254
AAC CGT TAC CTG GCT ATG AAG GAA GAT GGA AGA TTA CTG GCT TCT AAA TGT GTT ACG
Asn Arg Tyr Leu Ala Met Lys Glu Asp Gly Arg Leu Leu Ala Ser Lys Cys Val Thr
1269 1284 1299 1314
GAT GAG TGT TTC TTT TTT GAA CGA TTG GAA TCT AAT AAC TAC AAT ACT TAC CGG TCA
Asp Glu Cys Phe Phe Phe Glu Arg Leu Glu Ser Asn Asn Tyr Asn Thr Tyr Arg Ser
1329 1344 1359 1374
AGG AAA TAC ACC AGT TGG TAT GTG GCA TTG AAA CGA ACT GGG CAG TAT AAA CTT GGA
Arg Lys Tyr Thr Ser Trp Tyr Val Ala Leu Lys Arg Thr Gly Gln Tyr Lys Leu Gly
1389 1404 1419 1434
TCC AAA ACA GGA CCT GGG CAG AAA GCT ATA CTT TTT CTT CCA ATG TCT GCT AAG AGC
Ser Lys Thr Gly Pro Gly Gln Lys Ala Ile Leu Phe Leu Pro Met Ser Ala Lys Ser
1450 1460 1470 1480 1490 1500
TGA TTT TAATGGCTAT ATGTAAATGTG ATTTTGACATG AAAGAAGAAG TATATTCTAG AATATTTGTTA
1510 1520 1530 1540 1550 1560 1570
ATGAGAGTAA AAGAAAATAA ATGTGTATAG CTCAGTTTGG ATAATTGGTC AAACAATTTT TTATCCAGTA
1580 1590 1600 1610 1620 1630 1640
GTAAAATATG TAAGCATGCC GAGTAAAGAA AAATAACAAA AGTTGTAAAA TGTATATTGT GGCTTTTATA
1650 1660 1670 1680 1690 1700 1710
TTGCATCTGG TGTTAGGGAG TGAAGCTTAC GTAGAGCAAT GATCTTTTTG ACGCATTTGC TTTATTGGAA
1720 1730 1740 1750 1760 1770 1780
AAGAGGCTTT TAAAATGTGC ATGTTTAGAA AACAAAATTT CTTCATGGAA ATCATATACA TTAGAAAATC
1790 1800 1810 1820 1830 1840 1850
ACAGTGAGAC GTTTAATGAA TTGAAAAATG TGGACTATTT GTTATGTGAC TGGTTAGGGT ATATGTTTGT
1860 1870 1880 1890 1900 1910 1920
AAATATATAA ATGTGAATTT AATGAATTGC TTTGATAGTT TTATAATTGA GTGGGAGTGT GTTATGATAG
1930 1940 1950 1960 1969
ACTGTATAAA ACAGTGGTGT GTAAACTGGT CGAAGTTGTT CGGGAATTC

FIG. 2

Human Acidic FGF

```
                                                   27                                                  54
TGC ATT TTG TGC CTT TGC TGG AAG AAC CGA CTA CAG GTT TGT TCA ATT TGT TAC

                                                   81                                                 108
AGT CTT GAA AGC GCC ACA AGC AGC AGC TGC TGA GCC ATG GCT GAA GGG GAA ATC
                                                                MET Ala Glu Gly Glu Ile
                                                                 1

                                                  135                                                 162
ACC ACC TTC ACA GCC CTG ACC GAG AAG TTT AAT CTG CCT CCA GGG AAT TAC AAG
Thr Thr Phe Thr Ala Leu Thr Glu Lys Phe Asn Leu Pro Pro Gly Asn Tyr Lys
          10                                                  20

                                                  189                                                 216
AAG CCC AAA CTC CTC TAC TGT AGC AAC GGG GGC CAC TTC CTG AGG ATC CTT CCG
Lys Pro Lys Leu Leu Tyr Cys Ser Asn Gly Gly His Phe Leu Arg Ile Leu Pro
                    30                                            40

                                                  243                                                 270
GAT GGC ACA GTG GAT GGG ACA AGG GAC AGG AGC GAC CAG CAC ATT CAG CTG CAG
Asp Gly Thr Val Asp Gly Thr Arg Asp Arg Ser Asp Gln His Ile Gln Leu Gln
                          50                                            60

                                                  297                                                 324
CTC AGT GCG GAA AGC GTG GGG GAG GTG TAT ATA AAG AGT ACC GAG ACT GGC CAG
Leu Ser Ala Glu Ser Val Gly Glu Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln
                                70

                                                  351                                                 378
TAC TTG GCC ATG GAC ACC GAC GGG CTT TTA TAC GGC TCA CAG ACA CCA AAT GAG
Tyr Leu Ala MET Asp Thr Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro Asn Glu
      80                                            90

                                                  405                                                 432
GAA TGT TTG TTC CTG GAA AGG CTG GAG GAG AAC CAT TAC AAC ACC TAT ATA TCC
Glu Cys Leu Phe Leu Glu Arg Leu Glu Glu Asn His Tyr Asn Thr Tyr Ile Ser
          100                                           110

                                                  459                                                 486
AAA AAG CAT GCA GAG AAG AAT TGG TTT GTT GGC CTG AAG AAA AAT GGG AGC TGC
Lys Lys His Ala Glu Lys Asn Trp Phe Val Gly Leu Lys Lys Asn Gly Ser Cys
                    120                                           130

                                                  513                                                 540
AAA CGC GGT CCT CGG ACT CAC TAT GGC CAG AAA GCA ATC TTG TTT CTG CCA CTG
Lys Arg Gly Pro Arg Thr His Tyr Gly Gln Lys Ala Ile Leu Phe Leu Pro Leu
                          140                                           150

                                                  567                                                 594
CCA GTG TCT TCT GAT TAA AGA GAT GTC TTC TGC CTC ATT ATT CCA GAA AAA
Pro Val Ser Ser Asp
                    155

                                                  621
TTT CCA GGG GTC CCC AGT TGG TTG AGT GAA AAA TTT ...  ... CA
```

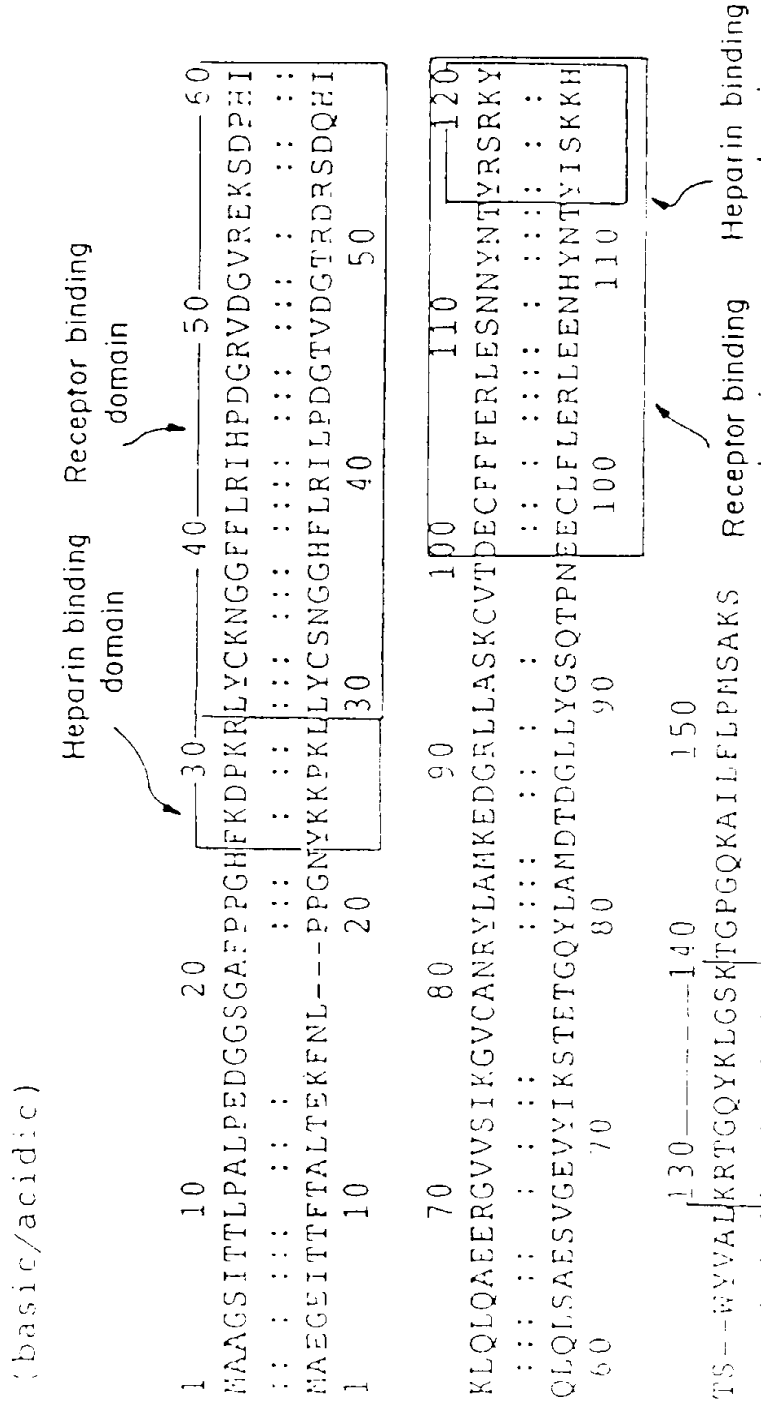
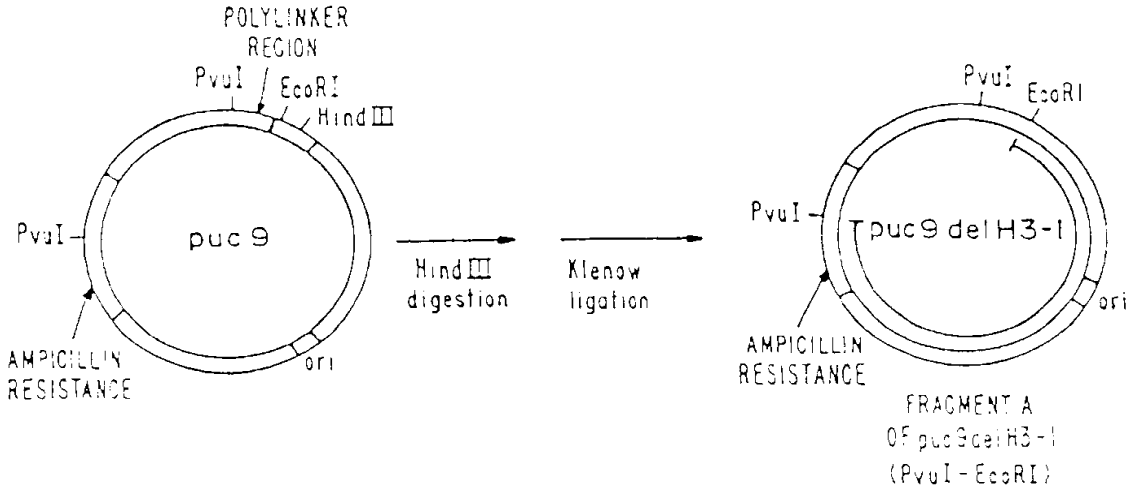

Comparison of amino acid sequence of human basic and acidic FGF
(basic/acidic)
Heparin binding domain
Receptor binding domain
Heparin binding domain
Receptor binding domain
Heparin binding domain

FIG. 3

EcoRI
-35
-10
mRNA START
SD
NdeI
KpnI
PstI
5' AGAATTCAAATATTCTGAAATGAGCTGTTGACAATTAATCATCGAACTAGTTAACTAGTACGCAAGTTCACGTAAAAAGGGTATCACATATGGTACCTGCAGA 3'
3' TCTTAAGTTTATAAGACTTTACTCGACAACTGTTAATTAGTAGCTTGATCAATTGATCATGCGTTCAAGTGCATTTTTCCCATAGTGTATACCATGGACGTCT 5'
1
2
3
4
5
6
7
8
9
10
pTRP-233
4.4 kb
Amp^R
PvuII
trp P/O
EcoRI
HindIII
PstI
KpnI
NdeI

FIG. 4


POLYLINKER REGION
PvuI
EcoRI
Hind III
PvuI
puc 9
AMPICILLIN RESISTANCE
ori
Hind III digestion
Klenow ligation
PvuI
EcoRI
PvuI
puc9 del H3-1
ori
AMPICILLIN RESISTANCE
FRAGMENT A OF puc9delH3-1 (PvuI-EcoRI)

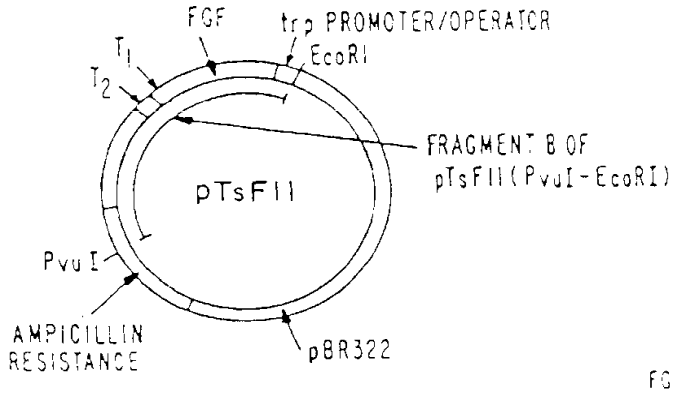
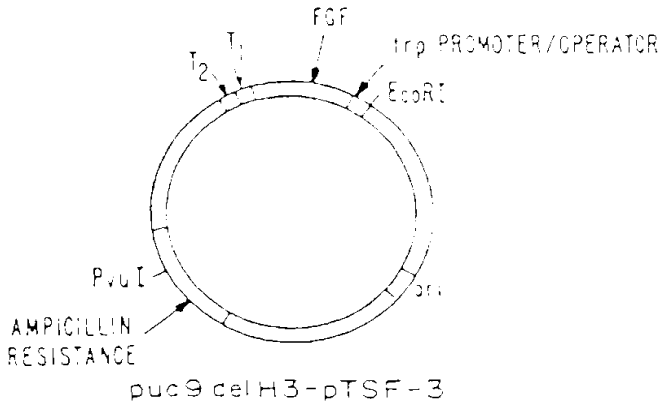

FGF
trp PROMOTER/OPERATOR
T1
T2
EcoRI
FRAGMENT B OF pTsF11 (PvuI-EcoRI)
pTsF11
PvuI
AMPICILLIN RESISTANCE
pBR322

FIG. 5


FGF
T1
T2
trp PROMOTER/OPERATOR
EcoRI
PvuI
AMPICILLIN RESISTANCE
puc9 delH3-pTSF-3

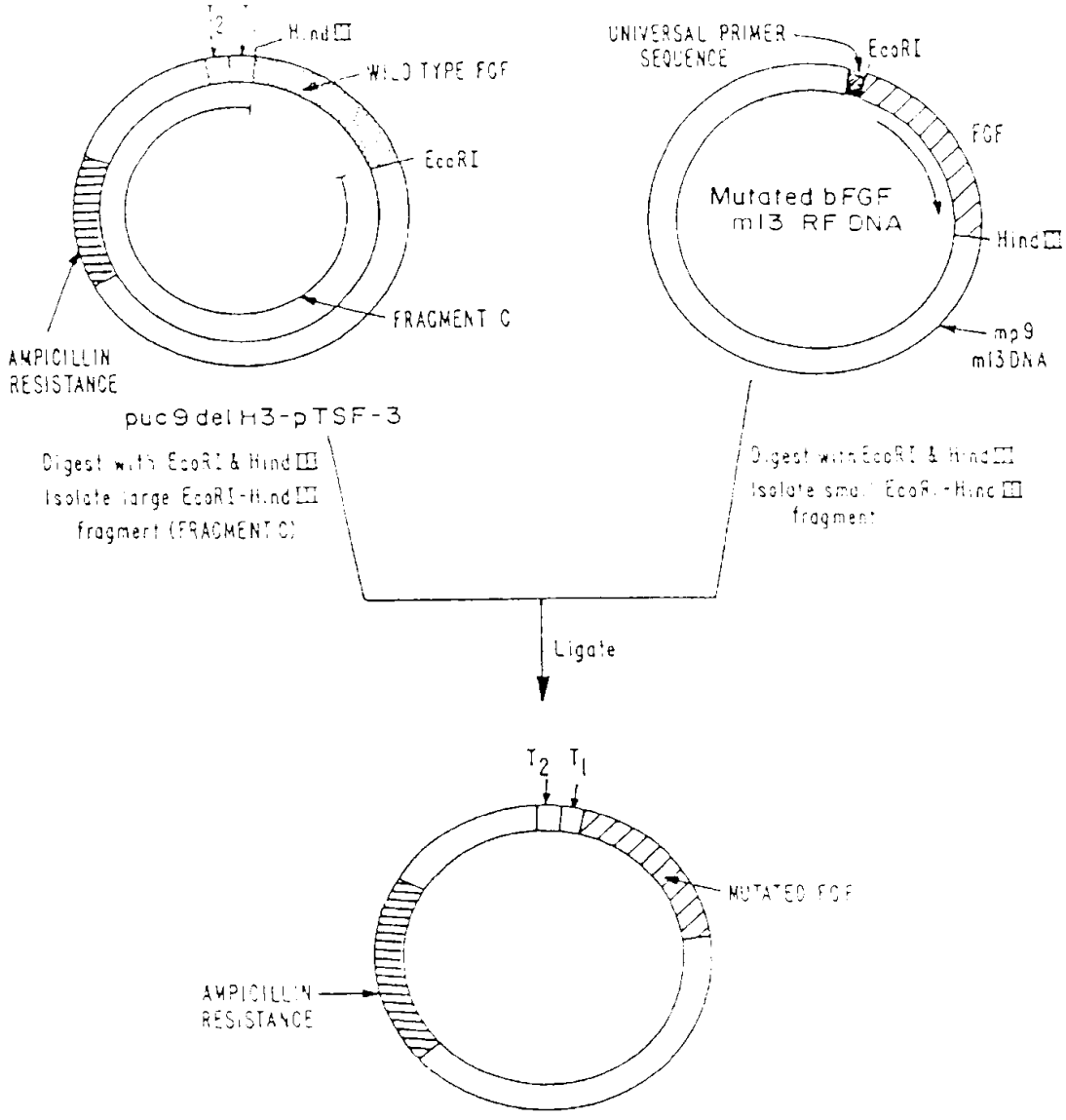

T2
HindIII
WILD TYPE FGF
EcoRI
FRAGMENT C
AMPICILLIN RESISTANCE
puc9 del H3-pTSF-3
Digest with EcoRI & HindIII
Isolate large EcoRI-HindIII fragment (FRAGMENT C)
UNIVERSAL PRIMER SEQUENCE
EcoRI
FGF
Mutated bFGF m13 RF DNA
HindIII
mp9 m13DNA
Digest with EcoRI & HindIII
Isolate small EcoRI-HindIII fragment
Ligate
T2
T1
MUTATED FGF
AMPICILLIN RESISTANCE

FIG. 6

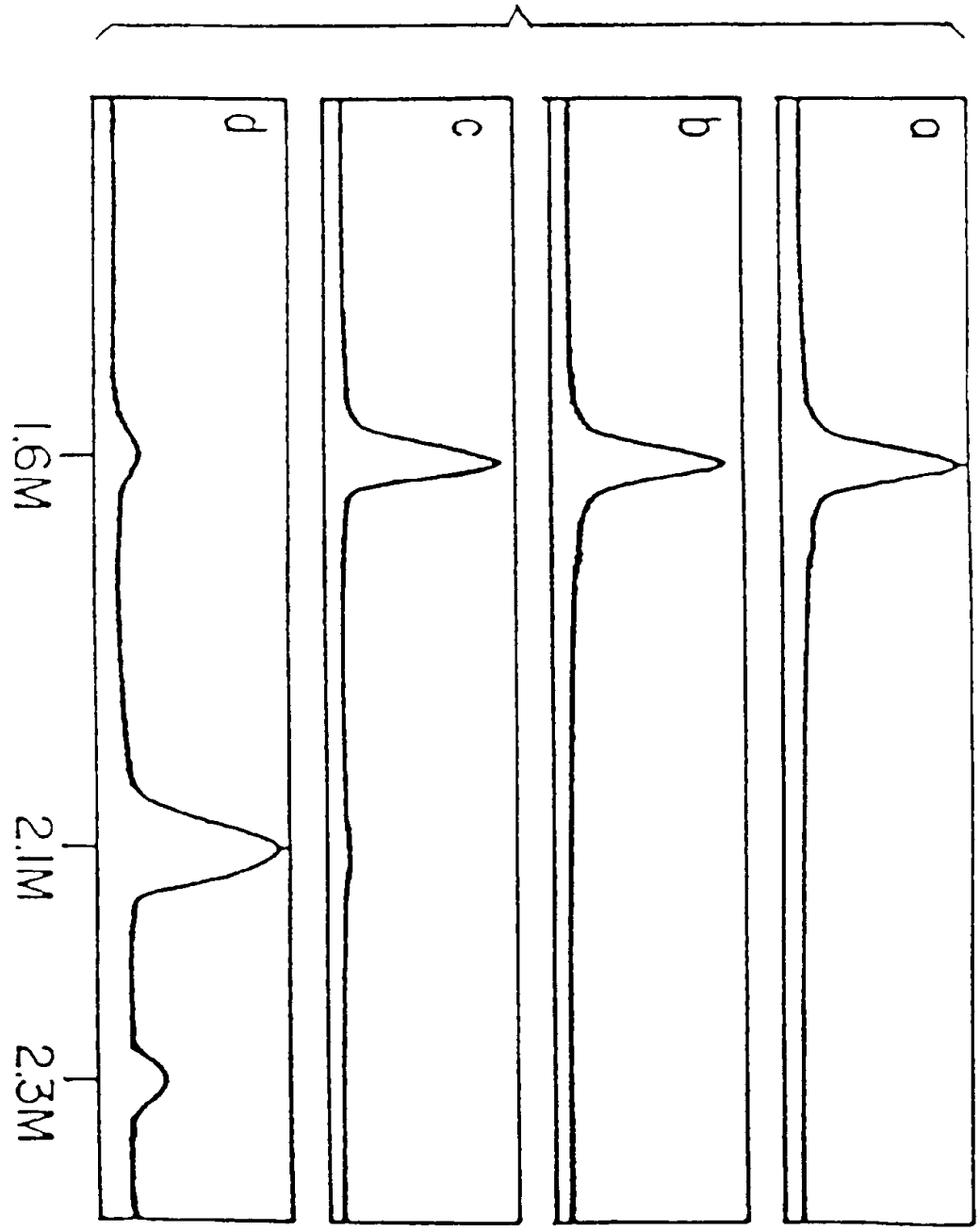



FIG. 7